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METHOD FOR MONITORING OF MEDICAL TREATMENT USING PULSE-ECHO ULTRASOUND

Inventor: *T. Douglas Mast*

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[0001]   **Field of the Invention**

[0002]   This is a continuation-in-part of Application No. 10/153,241, filed May 22, 2002, which claims priority to provisional application serial number 60/294,135 filed May 29, 2001. The present invention relates generally to ultrasound, and more particularly, to an ultrasound medical imaging method.

[0003]   **Background of the Invention**

[0004]   Ultrasound medical systems and methods include ultrasound imaging of anatomical tissue to identify tissue for medical treatment. Ultrasound may also be used to medically treat and destroy unwanted tissue by heating the tissue. Imaging is done using low-intensity ultrasound waves, while medical treatment is performed with high-intensity ultrasound waves. High-intensity ultrasound waves, when focused at a focal zone a distance away from the ultrasound source, will substantially medically affect tissue in the focal zone. However, the high-intensity ultrasound will not substantially affect patient tissue outside the focal zone, such as tissue located between the ultrasound source and the focal zone. Other treatment regimes of interest include unfocused high-intensity ultrasound, wherein the ultrasound energy is distributed over a relatively broad region of tissue rather than being generally concentrated within a focal zone.

[0005]   Ultrasound waves may be emitted and received by a transducer assembly. The transducer assembly may include a single element, or an array of elements acting together, to image the anatomical tissue and to ultrasonically ablate identified tissue. Transducer elements may employ a concave shape or an acoustic lens to focus ultrasound energy. Transducer arrays may include planar, concave or convex elements to focus or otherwise direct

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ultrasound energy. Further, such array elements may be electronically or mechanically controlled to steer and focus the ultrasound waves emitted by the array to a focal zone to provide three-dimensional medical ultrasound treatment of anatomical tissue. In some treatments the transducer is placed on the surface of the tissue for imaging and/or treatment of areas within the tissue. In other treatments the transducer is surrounded with a balloon which is expanded to contact the surface of the tissue by filling the balloon with a fluid such as a saline solution to provide acoustic coupling between the transducer and the tissue.

[0006]   Examples of ultrasound medical systems and methods include: deploying an end effector having an ultrasound transducer outside the body to break up kidney stones inside the body; endoscopically inserting an end effector having an ultrasound transducer into the rectum to medically destroy prostate cancer; laparoscopically inserting an end effector having an ultrasound transducer into the abdominal cavity to destroy a cancerous liver tumor; intravenously inserting a catheter end effector having an ultrasound transducer into a vein in the arm and moving the catheter to the heart to medically destroy diseased heart tissue; and interstitially inserting a needle end effector having an ultrasound transducer into the tongue to medically destroy tissue to reduce tongue volume as a treatment for snoring. Methods for guiding an end effector to the target tissue include x-rays, Magnetic Resonance Images ("MRI") and images produced using the ultrasound transducer itself.

[0007]   Low-intensity ultrasound energy may be applied to unexposed anatomical tissue for the purpose of examining the tissue. Ultrasound pulses are emitted, and returning echoes are measured to determine the characteristics of the unexposed tissue. Variations in tissue structure and tissue boundaries have varying acoustic impedances, resulting in variations in the strength of ultrasound echoes. A common ultrasound imaging technique is known in the art as "B-Mode" wherein either a single ultrasound transducer is articulated or an array of ultrasound transducers is moved or electronically scanned to generate a two-dimensional image of an area of tissue. The generated image is comprised of a plurality

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of pixels, each pixel corresponding to a portion of the tissue area being examined. The varying strength of the echoes is preferably translated to a proportional pixel brightness. A cathode ray tube or liquid crystal display can be used to display a two-dimensional pixellated image of the tissue area being examined.varying strength of the echoes is preferably translated to a proportional pixel brightness. A cathode ray tube or liquid crystal display can be used to display a two-dimensional pixellated image of the tissue area being examined.

[0008]   When high-intensity ultrasound energy is applied to anatomical tissue, significant beneficial physiological effects may be produced in the tissue. For example, undesired anatomical tissue may be ablated by heating the tissue with high-intensity ultrasound energy. By focusing the ultrasound energy at one or more specific focusing zones within the tissue, thermal effects can be confined to a defined region that may be remote from the ultrasound transducer. The use of high-intensity focused ultrasound to ablate tissue presents many advantages, including: reduced patient trauma and pain; potentially reduced patient recovery time; elimination of the need for some surgical incisions and stitches; reduced or obviated need for general anesthesia; reduced exposure of non-targeted internal tissue; reduced risk of infection and other complications; avoidance of damage to non-targeted tissue; avoidance of harmful cumulative effects from the ultrasound energy on the surrounding non-target tissue; reduced treatment costs; minimal blood loss; and the ability for ultrasound treatments to be performed at non-hospital sites and/or on an out-patient basis.

[0009]   Ultrasound treatment of anatomical tissue may involve the alternating use of both low-intensity imaging ultrasound and high-intensity treatment ultrasound. During such treatment, imaging is first performed to identify and locate the tissue to be treated. The identified tissue is then medically treated with high-intensity ultrasound energy for the purpose of ablating the tissue. After a period of exposure to high-intensity ultrasound, a subsequent image of the tissue is generated using low-intensity ultrasound energy to determine the results of the ultrasound treatment and provide visual guidance to the user

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to aid in subsequent treatments. This process of applying low-energy ultrasound to assist in guiding the position and focal point of the transducer, followed by high-energy ultrasound to ablate the undesired anatomical tissue, may continue until the undesired tissue has been completely ablated.

[0010] Although this conventional B-Mode ultrasound imaging provides an effective means for imaging tissue that is in a static state, imaging of the tissue becomes more problematic when used in conjunction with thermal high-intensity ultrasound treatment. As the tissue is ablated during treatment, the heating effects of ultrasound upon the tissue often result in qualitative changes in echo strength, causing brightness variations in the pixel display that do not consistently correspond spatially to the tissue being treated. These brightness variations result in an image display that does not represent the actual shape and size of the region of tissue that is being thermally modified by the treatment, introducing some visual ambiguity to the image.

[0011] Several methods are known for monitoring thermal ablation using B-Mode ultrasound imaging. Most of these are based on changes in the energy of ultrasound echoes, and include simple B-Mode displays of echo amplitude, estimates of tissue attenuation from analysis of distal shadowing, and quantification of changes in echo energy. Each of these methods have significant shortcomings because the tissue being treated can appear hyperechoic for reasons other than thermal ablation and because image changes must be qualitatively perceived by the user.

[0012] The most successful known methods for monitoring thermal ablation using ultrasound are based on analysis of changes in echo energy rather than a direct analysis of the echo energy. Automatic and quantitative displays of changes in echo energy or tissue attenuation are possible and can help users isolate thermally-induced changes from pre-existing echo characteristics. However, since such methods require integration of echoes over substantial regions of an image scan or "frame," the resulting images are very limited in spatial resolution. Although energy increases (and therefore B-Mode

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brightness increases) correspond roughly to lesion (i.e., the thermally treated tissue) position, typically the shape and size of the mapped energy increases do not always spatially correspond to actual lesions, and sometimes are either absent or otherwise unapparent.

[0013]   There is a need for an improved method of ultrasound imaging that can be utilized in conjunction with therapeutic ultrasound treatment that monitors the thermal effects of the treatment on targeted tissue with greater accuracy and resolution.

[0014]   **Summary of the Invention**

[0015]   The present invention overcomes the limitations of the known art by mapping differences between a first and second echo signal, each signal being obtained at different instants of time. The first and second signals are typically separated by a small time interval. The first and second signals are processed, then a measure of the amplitude of the differences between the first and second signals is made (as contrasted with a measure of the differences in signal amplitude). This difference signal is then spatially filtered and scaled to quantify echo changes associated with changes in tissue state. Difference signals may be summed over multiple time periods to obtain a cumulative map of the changes in the tissue. The resulting signals may be used to generate an ultrasound image that is more representative of the tissue as treatment progresses, providing additional information about where thermal effects are occurring. This allows for verification of successful treatment and modification of unsuccessful treatment. Known ultrasound imaging and treatment transducers may be used, providing users with increased accuracy without a need for special end effectors.

[0016]   **Brief Description of the Drawings**

[0017]   Further features of the present invention will become apparent to those skilled in the art to which the present invention relates from reading the following specification with reference to the accompanying drawings, in which:

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[0018]   Fig. 1 is a flow diagram providing an overview of an ultrasound treatment method according to an embodiment of the present invention;

[0019]   Fig. 2 illustrates the relative amplitude and timing of ultrasound image frames and ultrasound treatments of the method of Fig. 1;

[0020]   Fig. 3 is a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to an embodiment of the present invention;

[0021]   Fig. 4 is a view of a first ultrasound signal on a time scale;

[0022]   Fig. 5 is a view of a second ultrasound signal on a time scale;

[0023]   Fig. 6 is a composite view of the signals of Fig. 4 and Fig. 5;

[0024]   Fig. 7 is a view showing the difference signal computed from Fig. 4 and Fig. 5;

[0025]   Fig. 8 is a view showing the absolute value of the difference signal of Fig. 7;

[0026]   Fig. 9 is a view of the signal of Fig. 8 after filtering;

[0027]   Fig. 10 is a flow diagram depicting a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to an alternate embodiment of the present invention;

[0028]   Fig. 11 illustrates the relative amplitude and timing of ultrasound image frames, image frame sets and ultrasound treatments of the method of Fig. 10;

[0029]   Fig. 12 depicts a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to another alternate embodiment of the present invention;

[0030]   Fig. 13 shows the relative amplitude and timing of ultrasound image frame sets, difference signals and ultrasound treatments of the method of Fig. 12;

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[0031] Fig. 14 is a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to yet another alternate embodiment of the present invention; and

[0032] Fig. 15 shows the relative amplitude and timing of ultrasound image frames and ultrasound treatments of the method of Fig. 14.

[0033] <u>Detailed Description</u>

[0034] An overview of an ultrasound treatment method 10 according to an embodiment of the present invention is shown in Fig. 1. The method begins at step 12 by positioning proximate the targeted anatomical tissue to be medically treated a transducer capable of transmitting and receiving ultrasound signals. Once the transducer is in position, treatment begins at step 14 by emitting a high-intensity ultrasound signal from the transducer. The high-intensity ultrasound signal medically treats the targeted tissue, such as (but not limited to) heating the tissue to ablate the material. At step 16 a low-intensity ultrasound signal, such as a B-Mode signal, is emitted from the transducer and the reflected signals are received to form a first image frame F_1. It is understood that the terminology "image" includes, without limitation, creating an image in a visual form and displayed, for example, on a monitor, screen or display, and creating an image in electronic form which, for example, can be used by a computer without first being displayed in visual form. After the first image frame F_1 is received at step 16, a predetermined waiting period is executed at step 18 before proceeding further. It is to be understood that the predetermined waiting period may vary in value from zero seconds upwardly to a maximum of several seconds, but preferably is in the range of milliseconds. After the predetermined wait period has been completed, a low intensity ultrasound signal is again emitted from the transducer and a second image frame F_2 is received at step 20. At step 22 a difference signal is derived from the image frames F_1 and F_2, as will be discussed in greater detail below. The difference signal of step 22 is displayed as an image at step 24 to obtain a visual indication of the tissue change as a

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result of the medical treatment of step 14. It should be noted that the visual indication of the tissue change provided by the present invention differs from the post-treatment image of the prior art in that the present invention provides an image showing echo differences in contrast to echos from the target tissue. The image of echo differences can indicate whether treatment is complete. If treatment is complete at step 26 (for example, the targeted tissue has been fully ablated), the method is ended at step 28. However, if the tissue requires additional treatment, the transducer may be re-positioned at step 30. The method then returns to step 14 to continue medical treatment of the targeted tissue.

[0035]   Referring additionally to Fig. 2, the method of Fig. 1 is illustrated in relation to a time scale t. The targeted tissue is medically treated with a relatively high-intensity ultrasound signal as at step 14. Then, at step 16 a relatively low-intensity B-Mode image scan frame F_1 is received. After a predetermined off-time, as at step 18, a second image frame F2 is received, as at step 20. The image frames F_1 and F_2 each contain a signal representing the same portion of the target tissue. For each image frame, a number of A-lines of raw echo signal data are received, the number of each line corresponding to azimuthal position and the signal time corresponding to depth.

[0036]   Referring now to Fig. 3 in combination with Figs. 1 and 2, a method for monitoring medical treatment of anatomical tissue including, but not limited to, thermal ablation according to an embodiment of the present invention is depicted. An ultrasound transducer is positioned proximate the targeted anatomical tissue. The tissue may then be medically treated such as by ablation using high-intensity ultrasound waves for a period of time as at step 14. At step 16 a first image frame F_1 (such as is illustrated in Fig. 4) is received. The image frame may optionally be stored electronically, such as in a computer, magnetic media and solid-state memory. A second image frame F_2, separated from F_1 by a fixed time interval of step 18, is received at step 20. An example image frame F_2 is illustrated in Fig. 5. A difference signal is then derived at step 22 by means of steps 32-38. The raw echo signals of frames F_1 and F_2 may be processed at step 32, such as to obtain complex analytic signals by means of a Hilbert transformation. A

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difference signal may then be derived by subtracting the signal of image frame F_2 from the signal of F_1 at step 34. The difference signal of step 34 may take into account both phase and amplitude differences between F_1 and F_2, computing the amplitude of the signal differences (as opposed to differences in signal amplitude) of F_1 and F_2. A composite illustration of image frames F_1 and F_2 is shown in Fig. 6, while the derived difference signal is depicted in Fig. 7. At step 36 the difference signal may be scaled to a convenient value, such as the mean squared value of the difference signal, the mean squared value of one of the original echo signals, or a mathematical constant. As an example, a signal representing the scaled absolute value of the difference signal of Fig. 7 is shown in Fig. 8. Other functions of the difference signal, such as its squared absolute value or logarithm, may similarly be employed. Still other scaling algorithms may use the amplitude and/or phase of the first and second signals to enhance differences between the first and second signals. Details of such algorithms are left to the skilled artisan. At step 38 the difference signal is spatially filtered, as depicted in Fig. 9, to smooth small-scale random variations. Spatial filtering of the scaled difference signal is represented by Equation 1.

[0037] $$\Psi(x,z) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} w(x-x, z-z_0) \left| p_0(x_0, z_0) - p_1(x_0, z_0) \right|^2 dx_0 dz_0$$

[0038]   **Equation 1**

[0039]   In Equation 1 Ψ is a spatial difference map (image) of the scaled and filtered difference signal. The filtering may be performed by convolution of the scaled difference signal with a two-dimensional window w. This convolution may be efficiently performed through the use of two-dimensional Fast Fourier Transform ("FFT") operations.

[0040]   The difference signal may be normalized to have a maximum value of 1. This approach would result in a spatial map of the echo decorrelation, similar to measures of turbulence in color Doppler imaging systems. However, instead of examining echo decorrelation (a normalized measure of echo differences), a non-normalized map is considered preferable

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for the present invention because the echo difference is then enhanced in regions of greater echogenicity. Since hyperechoicity is one correlate to tissue ablation, this feature increases the specificity of the method for monitoring thermal ablative medical treatment by providing an image with greater detail.

[0041]   The spatially filtered signal of Fig. 9 is then displayed as an image at step 24 (see Fig. 3), in any manner previously discussed.

[0042]   In a second embodiment of the present invention, ultrasound images may be generated as depicted in Figs 10 and 11. At step 40 the tissue is medically treated with high-intensity ultrasound waves. At step 42 a succession of image frames, depicted as $F_1, F_2, ... F_n$, are received. The image frames $F_1, F_2, ... F_n$ each contain a signal representing the same portion of the target tissue. At step 44 the image frames $F_1, F_2, ... F_n$ are mathematically grouped, such as by summing or averaging, to form a first image frame set labeled FS_1, as shown in Fig. 11. After waiting a predetermined amount of time, as at step 46, a second set of image frames $F_1, F_2, ... F_n$ are received at step 48. At step 50 the second set of image frames $F_1, F_2, ... F_n$ are mathematically grouped, such as by summing or averaging, to form a second image frame set FS_2 as shown in Fig. 11. The raw echo signals of image frame sets FS_1 and FS_2 may be processed at step 52, such as to derive complex analytic signals by means of a Hilbert transformation. The signal of image frame set FS_2 is then subtracted from the signal of image frame set FS_1 at step 54 to derive a difference signal. The difference signal may take into account both phase and amplitude differences between FS_1 and FS_2, computing the amplitude of the signal differences (as opposed to differences in signal amplitude) of FS_1 and FS_2. At step 56 the difference signal may be scaled to a convenient value using any scaling methods and algorithms, previously described or otherwise. At step 58 the difference signal is spatially filtered to smooth small-scale random variations before being displayed as an image at step 59. This embodiment of the present invention may provide a more robust map of the backscatter changes by reducing the influence of random signal variations

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caused by rapid transient effects such as violent bubble activity produced during tissue ablation.

[0043]   In a third embodiment of the present invention, smoothing of the image signal may alternatively be accomplished by using a plurality of image frames, as illustrated in Figs. 12 and 13. The tissue is medically treated at step 60, then a set of image frames $F_1, F_2, ...$ F_n are received at step 62. A plurality of difference signals $D_1, D_2, ... D_n$ are computed at step 64. It should be noted that the difference signals may be computed using various arrangements of pairs of image frames. For example, difference signal D_1 may be formed by subtracting F_2 from F_1; likewise, D_2 may be formed by subtracting F_3 from F_2, as shown in Fig. 13. Other arrangements of image frame pairs may also be used, including (but not limited to) odd-numbered image frames (i.e., subtracting F_3 from F_1, etc.) and even-numbered image frames (i.e., subtracting F_4 from F_2, etc.). The pairings may be interlaced (i.e., subtracting F_2 from F_1, subtracting F_3 from F_2, etc.) or sequential (i.e., subtracting F_2 from F_1, F_4 from F_3, etc.). An indication or image may be displayed at step 66, showing at least one of the difference signals $D_1, D_2, ... D_n$. At step 68 the difference signals $D_1, D_2, ... D_n$ may be further processed, such as by averaging, to reduce artifactual content. The averaged signal, denoted as $\overline{D}$, may also be displayed as an image, as at step 70. The averaged signals may themselves be cumulatively summed, as at step 72, to provide a view of the results of successive medical treatments 60. The summed averages may be displayed at step 74. If treatment is determined to be complete at step 76, the method is ended at step 78. However, if the tissue appears to require additional treatment, the transducer may be re-positioned at step 80. The method is then repeated beginning at step 60 to continue treatment of the targeted tissue.

[0044]   A fourth embodiment of the present invention is shown in Figs. 14 and 15 wherein a difference signal is derived using imaging frames generated both before and after medical treatment. At step 82 the ultrasound transducer is positioned proximate the targeted tissue to be medically treated. At step 84 a pre-treatment image frame F_1 is generated from received ultrasound signals. Then, at step 86 the tissue is subject to a quantum of

medical treatment, such as by ablating the tissue. After a quantum of medical treatment is administered, a second image frame F_2 is generated at step 88. A difference signal is derived at step 90, using the data contained in image frames F_1 and F_2 in the same manner as previously described. An indication or image of the difference signal may be displayed at step 92. If treatment is determined to be complete at step 94, the method is ended at step 96. However, if the targeted tissue is determined to require additional treatment, the transducer may be re-positioned as necessary at step 98. The method is then repeated and a subsequent quantum of treatment is administered beginning at step 84.

[0045] An expected difficulty for the present invention is artifactual backscatter change due to tissue motion artifacts. This difficulty can be largely overcome by several features of the method. First, backscatter differences can be computed between image frames closely spaced in time. If the tissue moves only a small amount during the interval, motion artifacts are then small. Second, artifacts due to axial tissue motion can be removed effectively by phase compensation during signal processing. That is, before computation of the signal difference, one of the complex image frames is multiplied by a phase compensation function $e^{-i\theta}$, where θ is the low-pass filtered phase of the conjugate product of the two complex image frames. The resulting signal difference is then computed, for example, using Equation 2:

[0046] $$\Psi = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} w(x,z) \left| p_0(x,z) - p_1(x,z) e^{-i\varpi_0 \delta} \right|^2 dxdz$$

[0047] <u>Equation 2</u>

[0048] which is an improved echo difference map with reduced tissue motion artifacts.

[0049] It is understood that one or more of the previously-described embodiments, expressions of embodiments, examples, methods, etc. can be combined with any one or more of the other previously-described embodiments, expressions of embodiments, examples,

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methods, etc. For example, and without limitation, any of the ultrasound transducers may be used with other methods of medical treatment, such as producing images to aid in tissue ablation by means of Radio Frequency (RF) and laser energy, various non-ablative ultrasound medical treatments, and various ultrasound imaging applications.

[0050] The foregoing description of several expressions of embodiments and methods of the invention has been presented for purposes of illustration. It is not intended to be exhaustive or to limit the present invention to the precise forms and procedures disclosed, and obviously many modifications and variations are possible in light of the above teaching. It is intended that the scope the invention be defined by the claims appended hereto.

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